## (19) World Intellectual Property Organization

International Bureau



## 

(43) International Publication Date 1 September 2005 (01.09.2005)

(10) International Publication Number WO 2005/080316 A2

- (51) International Patent Classification<sup>7</sup>: C07C 233/68, 233/77, 63/04, 69/78, A61K 31/167, 31/192, 31/216, 31/235
- (21) International Application Number:

PCT/GB2005/000605

- (22) International Filing Date: 21 February 2005 (21.02.2005)
- (25) Filing Language:

English

(26) Publication Language:

English

(30) Priority Data:

0403864.2

20 February 2004 (20.02.2004)

- (71) Applicant (for all designated States except US): UNIVER-SITY COLLEGE LONDON [GB/GB]; Wolfson Institute for Biomedical Research, The Cruciform Building, Gower Street, London WC1E 6BT (GB).
- (72) Inventors; and
- (75) Inventors/Applicants (for US only): Masahiro [JP/JP]; Mitsubishi Pharma Corporation, 6-9, Hiranomachi, 2 Chome, Chuo-ku, Osaka 541-0046 (JP). SELWOOD, David [GB/GB]; Wolfson Institute for Biomedica Research, University College London, The Cruciform Building, Gower Street, London WC1E 6BT (GB). VISINTIN, Cristina [IT/GB]; Wolfson Institute for Biomedica Research, University College London, The Cruciform Building, Gower Street, London WC1E 6BT (GB). BAKER, David [GB/GB]; Department of Neuroinflammation, Institute of Neurology, University College London, 1 Wakefield Street, London WC1N 1PJ

(GB). PRYCE, Gareth [GB/GB]; Department of Neuroinflammation, Institute of Neurology, University College London, 1 Wakefield Street, London WC1N 1PJ (GB).

- (74) Agents: CLYDE-WATSON, Zoe et al.; D Young & Co, 120 Holborn, London EC1N 2DY (GB).
- (81) Designated States (unless otherwise indicated, for every kind of national protection available): AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN. TR. TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW.
- (84) Designated States (unless otherwise indicated, for every kind of regional protection available): ARIPO (BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW), Eurasian (AM, AZ, BY, KG, KZ, MD, RU, TJ, TM), European (AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR), OAPI (BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG).

## Published:

without international search report and to be republished upon receipt of that report

For two-letter codes and other abbreviations, refer to the "Guidance Notes on Codes and Abbreviations" appearing at the beginning of each regular issue of the PCT Gazette.

(54) Title: MODULATOR

(57) Abstract: The present invention relates to a compound of formula (I), or a pharmaceutically acceptable salt thereof, wherein Z is OR¹ or NR¹R² wherein each of R¹ and R² is independently H, or a hydrocarbyl group; X is an alkylene, alkenylene, or alkynylene group, each of which may be optionally substituted by one or more substituents selected from alkyl, COOH, CO₂-alkyl, alkenyl, CN, NHs, hydroxyl, halo allows CF, and alice Y or the substitution of the control o CN, NH<sub>2</sub>, hydroxy, halo, alkoxy, CF<sub>3</sub> and nitro; Y is a polar functional group selected from OH, NO<sub>2</sub>, CN, COR<sup>3</sup>, COOR<sup>3</sup>, NR<sup>3</sup>R<sup>4</sup>, CONR<sup>3</sup>R<sup>4</sup>, SO<sub>3</sub>H, SO<sub>2</sub>-R<sup>3</sup>, SO<sub>2</sub>NR<sup>3</sup>R<sup>4</sup> and CF<sub>3</sub>, where each of R<sup>3</sup> and R<sup>4</sup> is independently H or a hydrocarbyl group: A is an aryl or heteroaryl group, each of which may be optionally substituted; and B is (CH<sub>2</sub>)<sub>n</sub> where n is 0, 1, 2, 3, 4 or 5; with the proviso that: (i) when A is phenyl, n is 0, and Z is OH, X-Y is other than meta-C≡-C-(CH<sub>2</sub>)<sub>2</sub>CO<sub>2</sub>H, meta-C≡-C-(CH<sub>2</sub>)<sub>2</sub>OH, meta-C≡-C-(CH<sub>2</sub>)<sub>2</sub>CO<sub>2</sub>Me, meta-(CH<sub>2</sub>)<sub>4</sub>CO<sub>2</sub>H, ortho-CH<sub>2</sub>CO<sub>2</sub>H, ortho-(CH<sub>2</sub>)<sub>2</sub>CO<sub>2</sub>Hand ortho-(CH<sub>2</sub>)<sub>4</sub>CO<sub>2</sub>H; and (ii) when A is phenyl, n is 0, and Z is OMe. X-Y is other than meta-C≡C-(CH<sub>2</sub>)<sub>4</sub>OH. Further aspects of the invention relate to the use of such compounds in the preparation of a medicament for the treatment of a muscular disorder, a gastrointestinal disorder, or for controlling spasticity or tremors.